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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/009,011	07/19/2002	Jae-Hwan Nam	NIH256.001NP	2175

45311 7590 02/17/2005

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EXAMINER	
LUCAS, ZACHARIAH	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 02/17/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/009,011	NAM ET AL.	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 November 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *5, 7, 8, and 11-13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6,9,10,14-19 and 21* is/are rejected.

7)☒ Claim(s) *20* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12-4-01*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I (nucleic acids comprising a Bovine Viral Diarrhea Virus (BVDV) genome with a structural region of Hepatitis C Virus (HCV), and embodiments wherein the structural region is the HCV E2 protein encoding region) in the reply filed on November 26, 2004 is acknowledged.

The traversal is on the ground(s) that the restriction is improper insofar as it restricts embodiments encoding the E1 and E2 proteins because these proteins are disclosed in the art as functioning only as a heterodimer of the two proteins. This is not found persuasive because the claims are drawn to embodiments wherein a portion of the HCV genome encoding only one of the two proteins is required. Because the claims do not require the presence of both proteins in each embodiment, the Applicant arguments that the proteins may not be used separately are not found persuasive.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 5, 7, 8, and 11-13 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on November 26, 2004.

3. Claims 1, 2, 4, 6, 9, 10, 14-21 are under consideration to the extent that they read on, or are generic to, the elected invention.

Information Disclosure Statement

4. The information disclosure statement (IDS) submitted on December 4, 2001, is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has been considered by the examiner.

Claim Objections

5. Claim 1 is objected to because of the following informalities: the claim refers to the Bovine Viral Diarrhea Virus by its acronym (BVDV) without first identifying the virus by its complete name. It is suggested that the claim be amended such that the first appearance of BVDV be replaced to read as follows - - Bovine Viral Diarrhea Virus (BVDV)- -. Appropriate correction is required.

6. Claim 20 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim may not depend directly or indirectly from another multiple dependant claims. See MPEP § 608.01(n). In this case, claim 20 depends, indirectly, from multiple dependant claim 9. Accordingly, the claim has not been further treated on the merits.

Claim Rejections - 35 USC § 101

7. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

8. Claims 14, 15, 18, and 19 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. These claims read on any host cell transfected or infected to comprise the claimed nucleic acid. There is no requirement in the claims that the cell

is not a cell in a human organism. It is therefore suggested that the claims be amended to read on - - An isolated- - cell or host cell.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 1- 4, 6, 9, 10, 14-19, and 21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims read on compositions comprising a nucleic acid molecule comprising a chimeric BVDV genome in which a part of the viral genome has been replaced with that of HCV. Claim 1 appears to require that the entire BVDV structural region be replaced with the entire structural region of HCV. However, claim 2, which purports to further limit claim 1, indicates that only a single gene of the BVDV structural region is replaced with a corresponding gene of the HCV genome. It is therefore unclear whether the Applicant intended that claim 1 require the replacement of the entire BVDV structural region, or if the Applicant intended that the claim read on any BVDV virus wherein either the entire structural region or a single structural gene of the BVDV structural region be replaced by a corresponding portion of the HCV genome. I.e., claim 2 is not properly dependant on claim 1 as it appears to include subject matter that does not appear to fall within the scope of claim 1.

Clarification of the claim language is required.

For the purposes of this action, claim 1 is treated as reading on both substitutions of the entire structural region, and substitutions of individual structural genes, within the claimed chimeric BVDV genome.

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 16-19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for chimeric virus produced by a host cell infected by BVDV, and transfected by the DNA construct of claim 9 or 10, does not reasonably provide enablement for chimeric virus produced by any cell transfected with the indicated DNA constructs. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. The claims are drawn to chimeric virus that may be produced by any cell transfected with the BVDV/HCV chimeric genome described in claims 1 or 2.

However, in contrast to the breadth of these claims, the teachings of the application, and by a later reference, indicate that the chimeric virus may not be assembled in cells not also infected by non-chimeric BVDV. See, Application page 25 lines 6-10, and pages 27-28. See also, Nam et al., J Virol Methods 97: 113-23, at pages 118 (teaching that spread of virus occurred only in the bovine cell line infected by non-chimeric BVDV) and 121 (teaching that no chimeric virus spread was seen in infected human cell cultures, and hypothesizing that this was due to the lack of a helper BVDV). Thus, the application and the art indicate that chimeric virus

particles may only be produced by cells also infected by a non-chimeric BVDV. In view of the evidence presented by the application and art that chimeric virus may be produced only by such co-infected cells, and the lack of any evidence demonstrating that chimeric virus are produced by cells not so co-infected, the Applicant has not enabled those in the art to make or use chimeric virus produced by any cell transfected with only the DNA of claims 1 or 2.

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. Claims 1-4, 6, 9, 10, 14, 15, and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over the teachings of Vassilev et al. (J Virol 71: 471-78) in view of the teachings of Kashiwakuma et al. (J Immunol Methods 190: 79-89) and Maertens et al. (WO 96/04385). These claims read on nucleic acids comprising a chimeric BVDV genome in which the structural region of the genome, or a gene encoding a structural protein, has been substituted for the corresponding region of an HCV genome. Vassilev teaches a chimeric BVDV genome comprising a substitution of a non-structural region with a corresponding region of the HCV virus. The reference also suggests the use of BVDV as a viral vector for the expression of foreign proteins, and suggests substitutions such as those in the present claims. Page 477, last 2 paragraphs of text. Although the reference merely renders a chimeric virus of BVDV obvious to

try, those in the art would have had a reasonable expectation of success in the use of the virus as an expression vector.

The Kashiwakuma and Maertens references teach that the core, E1, and E2 HCV proteins are useful in diagnostics for HCV infection. In view of this, it would have been obvious to those in the art to use the BVDV genome as an expression vector for the production of HCV structural proteins, including the E2 protein. It would therefore have been obvious to those in the art to substitute the structural region of the BVDV protein for that of HCV in order to produce recombinant HCV proteins. The combined teachings of these references therefore render the claimed compositions obvious.

Conclusion

15. No claims are allowed.

16. The following prior art references are made of record and considered pertinent to applicant's disclosure. However, while relevant they are also not used as a basis for rejection for the stated reasons.

> Chambers et al., WO 98/37911. This reference teaches a chimeric yellow fever virus (a flavivirus) comprising a heterologous envelope virus of another flavivirus substituted for the yellow fever virus. Pages 4-5. Among the flaviviruses identified as supplying the heterologous envelope protein is HCV. However, the reference does not teach or suggest a chimeric BVDV.
>
> Hong et al. (U.S. 6,236,137). This reference teaches a chimeric BVDV virus in which a non-structural protein is substituted for an HCV protein. Column 4. However, the reference does not appear to teach substitution of structural BVDV proteins for those of HCV.
>
> Frolov et al., RNA 4: 1418-35. This reference teaches a chimeric BVDV genome comprising a portion of a HCV genome substituted for a correlating region of the BVDV region. However, the regions substituted are not structural genes. It is noted that the

references indicates that it would be of interest to make BVDV/HCV chimers of different genomic regions. Page 1431. However, the reference does not indicate that such viruses would be useful or viable. Thus, the reference renders the claimed chimeric molecules obvious to try, but not obvious to make.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 571-272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Z. Lucas
Patent Examiner

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